

AMENDMENTS TO THE DRAWINGS

Please replace Figure 22 with the Replacement Sheet for Figure 22.

Please replace Figure 25D with the Replacement Sheet for Figure 25D.

REMARKS

1. Formal Matters

a. Status of the Claims

Claims 1-24 are pending in this application. Claims 1-24 are hereby canceled without prejudice to pursuing these claims in a continuing application. Claims 25-38 are new. Upon entry of these amendments, claims 25-38 are pending and under active consideration. Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present application.

b. Amendments to the Claims

New claim 25 recites a nucleic acid consisting of 19 to 140 nucleotides, support for which may be found throughout the application including paragraphs 0041-0042 of the application as originally filed. New claim 25 also recites that the sequence of the nucleic acid may comprise at least 19 consecutive nucleotides of SEQ ID NO: 10068308, support for which may be found at Table 10, lines 738597-738604 of the application as originally filed. Table 10, lines 738594-738601 recites:

The GR12177 folded precursor RNA, herein designated GR FOLDED PRECURSOR RNA is naturally processed by cellular enzymatic activity into at least 5 separate GAM precursor RNAs GAM355613 precursor RNA, GAM355614 precursor RNA, GAM345990 precursor RNA, GAM355615 precursor RNA and GAM355616 precursor RNA, herein schematically represented by GAM1 FOLDED PRECURSOR RNA through GAM3 FOLDED PRECURSOR RNA. Each GAM folded precursor RNA is a hairpin-shaped RNA segment, corresponding to GAM FOLDED PRECURSOR RNA of Fig. 8.

SEQ ID NOS: 6842315, 6863394, 6821380, 6769403, and 6826827, all of which were disclosed in the application as originally filed, represent the sequences of GAM355613, GAM355614, GAM345990, GAM355615, and GAM355616, respectively. GAM355613 (SEQ ID NO: 6842315) is located on the plus strand of human chromosome 19 at positions 58,901,318 to 58,901,402 (See Table 2_A, lines 639,425-639,433). GAM355614 (SEQ ID NO: 6863394) is located on the plus strand of human chromosome 19 at positions 58,902,519 to 58,902,605 (See Table 2_A, lines 639,521-639,529). GAM345990 (SEQ ID NO: 6821380) is located on the plus strand of human chromosome 19 at positions 58,903,813 to 58,903,818 (See Table 2_A, lines

144,985-144,993). GAM355615 (SEQ ID NO: 6769403) is located on the plus strand of human chromosome 19 at positions 58,907,334 to 58,907,420 (See Table 2_A, lines 639,617-639,625). GAM355616 (SEQ ID NO: 6826827) is located on the plus strand of human chromosome 19 at positions 58,908,413 to 58,908,500 (See Table 2_A, lines 639,713-639,721).

SEQ ID NO: 10068308 (GR12177) represents the sequence of the plus strand of human chromosome 19 at positions 58,901,318 to 58,908,500 (See amended Table 10, lines 738,588-738,589). Therefore, SEQ ID NO: 10068308 (GR12177) is defined by the following (beginning at the 5' end): the sequence of GAM 355613 (SEQ ID NO: 6842315); the intervening 1116 base pairs between GAM355613 and GAM355614; the sequence of GAM355614 (SEQ ID NO: 6863394); the intervening 1204 base pairs between GAM355614 and GAM345990; the sequence of GAM345990 (SEQ ID NO: 6821380); the intervening 3437 base pairs between GAM345990 and GAM355615; the sequence of GAM355615 (SEQ ID NO: 6769403); the intervening 992 base pairs between GAM355615 and GAM355616; and the sequence of GAM355616 (SEQ ID NO: 6826827).

New claim 25 also recites that the nucleic acid may be an RNA equivalent of (a), support for which may be found in the application as originally filed including at paragraph Table 2_A, lines 144957-145050, 639397-639490, 639493-639586, 639589-639682, and 639685-639778 of the application as originally filed.

New claim 25 is further directed to a nucleic acid that may be: a sequence at least 80% identical to (a) or (b), support for which may be found at paragraph 0046 of the application as originally filed.

New claim 25 further recites that the nucleic acid may be: the complement of any one of (a)-(c), support for which may be found at Table 2_A, lines 144957-145050, 639397-639490, 639493-639586, 639589-639682, and 639685-639778 of the application as originally filed.

New claim 26 is directed to the nucleic acid of claim 25, wherein the at least 19 nucleotides is of a sequence selected from the group consisting of SEQ ID NOS: 6769403, 6821380, 6826827, 6842315, and 6863394, support for which can be found at Table 2_A, lines 144957-145050, 639397-639490, 639493-639586, 639589-639682, and 639685-639778 of the application as originally filed.

New claim 27 recites the nucleic acid of claim 25, wherein the at least 19 nucleotides is of a sequence selected from the group consisting of SEQ ID NOS: 45, 159, 1166, 3201, and

7870, support for which can be found at Table 1, lines 19008, 342, 94, 2750, and 7624 of the application as originally filed.

New claim 28 is directed to a nucleic acid of claim 25, wherein the nucleic acid consists of 19 to 24 nucleotides, support for which can be found at paragraph 0042 of the application as originally filed.

New claim 29 recites a nucleic acid with a sequence consisting of (a) at least 19 consecutive nucleotides of SEQ ID NO: 10068308; (b) an RNA equivalent of (a); (c) a sequence at least 80% identical to (a) or (b); or (d) the complement of any one of (a)-(c), support for which may be found as described above for new claim 25.

New claim 30 is directed to a nucleic acid of claim 29, wherein the at least 19 nucleotides is of a sequence selected from the group consisting of SEQ ID NOS: 6769403, 6821380, 6826827, 6842315, and 6863394, support for which can be found as described for new claim 26.

New claim 31 recites the nucleic acid of claim 29, wherein the at least 19 nucleotides is of a sequence selected from the group consisting of SEQ ID NOS: 45, 159, 1166, 3201, and 7870, support for which can be found as described for new claim 27.

New claim 32 is directed to a nucleic acid of claim 29, wherein the nucleic acid consists of 19 to 24 nucleotides, support for which can be found as described for new claim 28.

New claim 33 recites a nucleic acid of claim 26, wherein the nucleic acid is an RNA, support for which can be found at paragraph Table 2_A, lines 144957-145050, 639397-639490, 639493-639586, 639589-639682, and 639685-639778 of the application as originally filed.

New claim 34 is directed to a nucleic acid of claim 30 wherein the nucleic acid is an RNA, support for which can be found at paragraph Table 2_A, lines 144957-145050, 639397-639490, 639493-639586, 639589-639682, and 639685-639778 of the application as originally filed.

New claim 35 recites a vector comprising an insert, wherein an insert consists of the nucleic acid of claim 25, support for which can be found at paragraph 0027 of the application as filed.

New claim 36 is directed to a vector comprising an insert, wherein an insert consists of the nucleic acid of claim 29, support for which can be found at paragraph 0027 of the application as filed.

New claim 37 recites a probe comprising an insert, wherein an insert consists of the nucleic acid of claim 25, support for which can be found at paragraph 0027 of the application as originally filed.

New claim 38 is directed to a probe comprising an insert, wherein an insert consists of the nucleic acid of claim 29, support for which can be found at paragraph 0027 of the application as originally filed.

c. Amendments to the Specification

Paragraph 0263 is amended to assign SEQ ID NOS: 10068286-10068296 to the sequences shown in Fig. 23A in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraph 0266 is amended to assign SEQ ID NOS: 10068281-10068285 to the sequences shown in Fig. 24A in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraph 0452 is amended to assign SEQ ID NOS: 10068309-10068313 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraphs 0467-0469 are amended to assign SEQ ID NOS: 10068314-10068319 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraph 0471 is amended to assign SEQ ID NOS: 10068320-10068322 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraph 0496 is amended to assign SEQ ID NOS: 10068178-10068183 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraph 0499 is amended to assign SEQ ID NOS: 10068184-10068185 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraphs 0559-0579 are amended to assign SEQ ID NOS: 10068186-10068193 and 10068306-10068307 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

Table 10, lines 738586-738597 is amended to recite that human GR12177 is located from position 58901318 to 58908500, support for which may be found at Table 2_A, lines 639428-639433, 639524-639529, 144988-144993, 639620-639625, 639716-639721, and Table 10, lines 738586-738603 of the application as originally filed.

As described hereinabove in Section 1b, Table 10, lines 738597-738603 discloses that GR12177 (SEQ ID NO: 10068308) encodes an RNA that is processed into at least five precursor RNAs, including GAM355613, GAM355614, GAM345990, GAM355615, and GAM355616, respectively. GAM355613 is located on the plus strand of human chromosome 19 at positions

58,901,318 to 58,901,402 (See Table 2_A, lines 639,425-639,433). GAM355616 is located on the plus strand of human chromosome 19 at positions 58,908,413 to 58,908,500 (See Table 2_A, lines 639,713-639,721). If GR12177 (SEQ ID NO: 10068308) encodes GAM355613 and GAM355616, then GR12177 can not only be located “from position 58,908,413 to 58,908,500 on the ‘+’ strand of chromosome 19” as recited at Table 10, lines 738588-738589. Instead, GR12177 must be located on the plus strand of human chromosome 19 at least from position 58,901,318, which is the 5’ end of GAM355613, to position 58,908,500, which is the 3’ end of GAM355616. Therefore, Applicant respectfully submits that the recitation of “position 58,908,413” at Table 10, line 738588, which describes the 5’ end of GR12177, is clearly a typographical error and should have recited “position 58,901,318” as supported by the application as originally filed. Applicant respectfully submits that the amendment to Table 10, lines 738586-738597 does not introduce new matter and is supported by the application as originally filed.

d. Amendments to the Drawings

Figure 22 is amended by replacing it with a Replacement Sheet for Fig. 22 to assign SEQ ID NOS: 10068194-10068280, and 10068323-10068324 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

Figure 25D is amended by replacing it with a Replacement Sheet for Fig. 25D to assign SEQ ID NOS: 10068297-10068305 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825. No new matter has been added.

e. Notice to Comply with Sequence Rules

On page 2 of the Office Action, the Examiner alleges that the specification and sequence listing do not comply with 37 C.F.R. §§ 1.821-1.825. Specifically, the Examiner alleges that sequence identifiers are not associated with sequences disclosed in Figures 22, 23, and 25, and paragraphs 0496, 0499, and 0559-0579.

Applicant submits herewith a replacement sequence listing pursuant to 37 C.F.R. § 1.825(a), and the specification and drawings are amended throughout to disclose the appropriate SEQ ID NOS in accordance with 37 C.F.R. §§ 1.821-1.825. No new matter has been added.

In light of the amendments to the specification described hereinabove, and the replacement drawings and replacement sequence listing submitted herewith, Applicant respectfully submits that the application is in compliance with 37 C.F.R. §§ 1.821-1.825.

f. Election/Restrictions

On pages 3-6 of the Office Action, the Examiner requires restriction to one of the following inventions under 35 U.S.C. § 121:

- I. Claims 1-11 and 20-23, drawn to a bioinformatically detectable isolated oligonucleotide, which anneals to a portion of a mRNA transcript of target gene, and which modulates or represses expression of said target gene.
- II. Claims 12, 16, and 17, drawn to a method of treatment of a disease, comprising providing a material that modulates or inhibits the activity of a microRNA, and to methods thereof wherein the material is an oligonucleotide.
- III. Claims 13-15, drawn to a method for treatment of a disease, comprising providing a material that binds a segment of a mRNA and inhibits the expression of protein from said mRNA, and to methods thereof wherein the material is a microRNA.
- IV. Claims 18 and 19, drawn to a method for diagnosis of a disease, comprising assaying a microRNA, and to a method for detection of expression of an oligonucleotide.
- V. Claim 24, drawn to a method for bioinformatic detection of microRNA.

Applicant elects without traverse Group I, which now is considered claims 25-38, drawn to an isolated nucleic acid, a vector comprising the nucleic acid, and a probe comprising the nucleic acid.

g. Restriction to a Single Nucleotide Sequence and mRNA target gene

On pages 6-9 of the Office Action, the Examiner requires restriction to a single nucleic acid sequence for the elected Group I under 35 U.S.C. § 121. Applicant elects with traverse nucleic acids related to SEQ ID NO: 10068308, which is associated with claims 25-38 for further prosecution.

The Examiner is permitted under 35 U.S.C. § 121 to issue a restriction requirement between independent and distinct inventions. However, the Director has partially waived the requirements of 37 C.F.R. § 1.141 *et seq.* to permit a reasonable number of nucleotide sequences

to be claimed in a single application. *See* Examination of Patent Applications Containing Nucleotide Sequence, 1192 O.G. 68 (November 19, 1996). It has been determined that normally **ten** sequences constitute a reasonable number for examination purposes absent an exceptional case. *See* MPEP 803.04.

The Examiner has failed to demonstrate that the claimed sequences are an exceptional case necessitating that the number of sequences to be selected be less than ten. Applicant respectfully submits that the Examiner is impermissibly disregarding the waiver of 37 C.F.R. § 1.141 *et seq.* Accordingly, Applicant respectfully requests reconsideration of the restriction requirement and the opportunity to elect up to ten sequences for further prosecution.

h. Species Election Regarding Target Genes in Group I

On page 8 of the Office Action, the Examiner requires election of a single disclosed target gene species for Group I under 35 U.S.C. § 121. Applicant elects without traverse the target gene EGFR, which has the sequence SEQ ID NO: 783894.

2. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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